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Document Number 41

Entry 41 of 53

File: USPT

Jan 3, 1995

DOCUMENT-IDENTIFIER: US 5378464 A

TITLE: Modulation of inflammatory responses by administration of GMP-140 or antibody to GMP-140

DEPR:

Other studies have demonstrated that GMP-140 binds to C3b, a complement system protein, and protein S, an anticoagulant cofactor protein. GMP-140 shares sequence homology with the plasma protein C4b-binding protein (C4bp), which not only interacts with the plasma protein C4b but also with protein S.

DEPR:

One of the complement-regulatory proteins containing repeating units homologous to those in GMP-140 is C4b-binding protein (C4bp). In addition to binding C4b, this plasma protein also binds the anticoagulant cofactor, protein S. Protein S serves as a cofactor for the anticoagulant serine protease, activated protein C. Activated protein C proteolytically inactivates coagulation Factors V and VIII, thus suppressing the coagulation cascade. Binding of protein S to C4bp blocks the anticoagulant functions of protein S. The dual binding specifications of C4bp for C4b and protein S suggested that GMP-140 might also bind protein S. This possibility was especially attractive because certain vascular cell receptors such as Mac-1 on monocytes can have several different functions related to both inflammation and coagulation. A number of studies have now shown that purified GMP-140 does interact with purified protein S. Initial studies suggest that the binding facilitates the anticoagulant cofactor function of protein S. Accordingly, infusion of soluble fragments of GMP-140 containing the protein S-binding site might serve as novel anticoagulants.

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